

AMENDMENTS

IN THE SPECIFICATION

Please insert the attached "Sequence Listing" as separately numbered pages 1-3 after the abstract.

Replace paragraphs 20 and 21 in their entirety with the following paragraphs:

[020] Figures 2A-2C: Schematic representation of the DOG/SOG gene and protein. A) The DOG gene contains 7 exons with a translation initiation site in the first exon. The SOG transcript is produced from the same transcription start site but utilizes an AUG codon located on the second exon and in a different reading frame from that of DOG. In addition, the lack of splicing between exons 4 and 5 causes a frame-shift back to the same reading frame as DOG. B,C) Utilization of an AUG in a different frame causes SOG to lose the entire core of the DOG OTU catalytic domain. The frame-shift caused by the read-through of the intron between exons 4 and 5 results in a protein (SOG) that has a c-terminus identical to that of DOG. Figure 2C provides an alignment of SEQ ID NO:9 and SEQ ID NO:10.

[021] Figures 3A-3C. Binding of DOG and SOG to GRAIL does not require an intact RING domain. A) Linearized plasmids encoding either DOG or SOG were used as templates in a combined transcription/translation reaction using a rabbit reticulocyte lysate system (T7-TNT, Promega) and 35S-Met. A portion of the completed reaction was incubated with either recombinant GST-GRAIL fusion protein or GST alone under agitation for 4 hours. Complexes were captured with glutathione-agarose beads, washed several times and eluted with reduced glutathione. Eluted proteins were subjected to electrophoresis and the dried gel exposed to film. B) HEK 293 cells were co-transfected with plasmids coding for GRAIL tagged with V5 and either DOG or SOG, tagged with HSV. GRAIL was immunoprecipitated with anti-V5 antibody and the immunocomplexes were resolved by electrophoresis and transferred to PVDF membranes. Immunoblot was carried-out with anti-HSV and anti-V5 antibodies. C) Liver tissue extracts (5 mg) were immunoprecipitated with polyclonal antibodies to either GRAIL or DOG. A pre-immune rabbit antiserum was used as control. Immunoprecipitates were resolved by SDS-PAGE, transferred to PVDF and immunoblotted with a GRAIL-specific monoclonal antibody.